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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/009,802	01/20/1998	SEAN MCCARTHY	1855.2067-000	7895

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EXAMINER	
GUZO, DAVID	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/009,802	MCCARTHY, SEAN	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/12/04 has been entered.

Claims 61-88 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

This rejection is maintained for reasons of record in the previous Office Action (mailed 4/9/03) and for reasons outlined below.

Applicant traverses this rejection by asserting that the examiner improperly appears to be looking for an assertion of utility that has a degree of particularity that amounts to disclosure of how or why the invention works, e.g., the molecular interactions or mechanisms underlying the utility of CRSP-2. Applicant indicates that this level of detail is not required by the patent statutes. Applicant indicates that CRSP proteins, including CRSP-2, can have any one of six different properties biological properties outlined in the specification and that these represent specific and substantial asserted utilities. It is asserted that CRSP proteins and CRSP-2 in particular can be

used to study mechanisms underlying development and differentiation of cells and tissues and can be viewed as research tools for regulating cell proliferation. Applicant asserts that this represents a specific and substantial utility because further research on the claimed polypeptide is not necessary to identify or confirm this use. Applicant asserts that the examiner has not presented any evidence that the recited utilities are merely general utilities applicable to a broad class of subject matter.

With regard to the outstanding 112, 1st paragraph (enablement) rejection of claims 61-88, applicant indicates that this rejection is based solely upon the examiner's opinion that the invention does not satisfy the utility requirement.

Applicant's arguments filed 5/12/04 have been fully considered but they are not persuasive. The examiner is not requiring applicant to disclose how the invention works, only to disclose a specific and substantial utility for the claimed invention. Mere membership in a class of compounds (CRSPs) does not translate into a specific utility for the claimed species (CRSP-2) because one of skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based upon knowledge of the class of compounds of which the claimed species is a member. In the instant case, applicant provides no disclosure of any **specific biological properties** of any member of the CRSP group of proteins, only vague generalities concerning the possible involvement of CRSPs in modulation of signal transduction, regulation of gene transcription in a cell involved in development or differentiation, etc. Applicant is asserting that CRSP proteins could be involved in any of hundreds of different cellular pathways or are involved in some undisclosed fashion with any of thousands of different

genes regulating development, differentiation and proliferation of cells. Attempting to assign a **specific and substantial utility** to CRSP-2 based upon its inclusion in this group of proteins is purely guesswork.

Applicant lists a series of six generic activities that the class of CRSP proteins have. No **specific biological properties** of CRSP-2, or indeed, any other CRSP are listed. No specific signal transduction pathway modulated by CRSP-2 is disclosed, no gene target of CRSP-2 in any cell is disclosed, no effect(s) exerted by CRSP-2 on regulation of gene expression in any cell or tissue is disclosed, no role in cellular differentiation mediated by CRSP-2 is disclosed, no role in the regulation of any specific gene encoding a differentiation-specific or development-specific protein is disclosed, etc. Thus applicant discloses no practical, real world, use for the claimed protein wherein said use provides a benefit **in currently available form**. Indeed, in order to develop a real world, practical, utility for the claimed protein, the skilled artisan would need to conduct further research on the protein itself in order to determine what specific utility it possesses in affecting gene expression in any given human cell or tissue. With regard to applicant's assertion that later disclosures have provided a utility for the claimed protein and that this utility is supported by the specification, it is noted that the only function associated with CRSP-2 which is elucidated in said later disclosures involves cooperating in some undisclosed manner with Krm2 protein to inhibit Wnt signaling in 293 cells. The specification, as filed, does not provide support for this utility. Indeed, years of further research on the CRSP-2 (Dkk4) protein was required to

ascertain even this limited concept of what biological functions CRSP-2 actually performs in humans.

Claims 61-88 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial or well established utility asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

This rejection is maintained given the lack of a specific, substantial or well established utility for the claimed invention.

Claims 61-69, 76-85 and 87-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims isolated polypeptides comprising an amino acid sequence at least 80% or at least 90% identical to SEQ ID NO:5 (CRSP-2) or at least 80% or 90% identical to specific portions of SEQ ID NO:5 or polypeptides having various consecutive amino acid residues of SEQ ID NO:5 or isolated polypeptides encoded by nucleic acid sequences capable of hybridizing to SEQ ID NO: 4 or 6 under specific conditions or a pharmaceutical composition comprising said polypeptides or fusion proteins comprising SEQ ID NO:5 (or portions thereof or homologous sequences) and a carrier or a method for identifying a compound that modulates the activity of a CRSP protein, comprising:

providing a indicator composition comprising a protein having CRSP-2 activity; contacting the indicator composition with a test compound; and determining the effects of the test compound on CRSP-2 activity in the indicator composition to thereby identify a compound that modulates the activity of an CRSP-2 protein.

This enablement rejection will address three separate areas. 1. Enablement for polypeptides which are homologous to or contain portions of SEQ ID NO:5 or are encoded by nucleic acid sequences capable of hybridizing to sequences encoding SEQ ID NO:5; wherein said polypeptides are claimed without a recited function. 2. Enablement for pharmaceutical compositions comprising the recited polypeptide and 3. Enablement for a method for identifying compounds that modulate the activity of CRSP-2.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reaches by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art with regard to how to make and use polypeptides which are at least 80% or 90% homologous to or comprise portions of or are capable of hybridizing to SEQ ID NO:5 and which do not have the biological functions of SEQ ID NO:5 is unpredictable. Indeed, generally the art is unpredictable

with regard to how to make and use polypeptides which are homologous at a certain level or comprise portions of a recited polypeptide or are encoded by nucleic acids capable of hybridizing to a sequence encoding a given polypeptide when the polypeptides are not recited as having the biological function(s) of the original polypeptide because the claim reads on polypeptides which have undisclosed or unrelated or no function and applicant has not disclosed how to use these molecules. In the instant case, since applicant has not disclosed any specific biological functions associated with CRSP-2, it is unclear how applicants would use polypeptides comprising portions of SEQ ID NO:5 or polypeptides at least 80% or 90% identical to SEQ ID NO:5, etc.

With regard to pharmaceutical compositions comprising SEQ ID NO:5 or molecules homologous thereto or comprising portions of SEQ ID NO:5 or polypeptides encoded by sequences capable of hybridizing to sequences encoding SEQ ID NO:5, applicant has provided no disclosure of any specific diseases associated with expression of SEQ ID NO:5 or associated with under, or over, expression of SEQ ID NO:5. Applicant has provided no disclosure of how one of skill in the art would treat any given disease condition with SEQ ID NO:5 or sequences related in the recited fashions to said molecule. Applicant presents no disclosure on the dosages of SEQ ID NO:5, or polypeptides related thereto for treating any specific disease, the dosages of any agonists or antagonists of SEQ ID NO:5 so as to treat any disease associated with under, or over, expression of SEQ ID NO:5, etc. Attempting to treat diseases by administering a polypeptide, the functions of which *in vivo* are unknown, or which is not

known to be associated with said diseases or associated with said diseases in some undisclosed fashion must be considered unpredictable.

With regard to the claimed method of identifying a compound that modulates the activity of CRSP-2, since applicant does not disclose any specific activity of CRSP-2, it is unclear how applicant would determine the effect of a test compound on the activity of CRSP-2. The skilled artisan would need to perform extensive additional experimentation on CRSP-2 itself to ascertain the biological activities of CRSP-2 before said artisan could even begin to test compounds for their ability to modulate the activity of CRSP-2. For example, the skilled artisan would need to know the signal pathways affected by expression of CRSP-2, the genes activated or repressed by CRSP-2, the ligands associated with CRSP-2, etc. in order to develop some sort of intelligent screening method for identifying compounds capable of modulating the activity of CRSP-2. A method for testing the ability of compounds to modulate the biological activity of a polypeptide, the biological activities of which are unknown, must be considered unpredictable since it would involve trial and error experimentation in the absence of data on the specific biological activities of the CRSP-2 polypeptide.

2) State of the art. The state of the art with regard to use of CRSP-2 as a pharmaceutical agent for treatment of disease is nil. The state of the art with regard to the biological activities of CRSP-2 is poorly developed as it was unknown what specific biological activities it possessed. The state of the art with regard to polypeptides which have homologies to SEQ ID NO:5 or have portions of SEQ ID NO:5 but not the functions of SEQ ID NO:5 is nil. The state of the art with regard to methods for

identifying compounds that modulate the activity of CRSP-2, in the absence of data on the specific biological activities of CRSP-2, is nil.

3) Number of working examples. Applicants present no working examples of pharmaceutical compositions comprising SEQ ID NO:5 or portions thereof or sequences homologous thereto. Applicants present no working examples of a method for identifying any compound that modulates the activity of CRSP-2. Applicants present no working examples of how to make and use any polypeptides which are homologous to (at least 80 or 90%) SEQ ID NO:5 or comprise portions of SEQ ID NO:5 or are encoded by nucleic acids capable of hybridizing to sequences encoding SEQ ID NO:5.

4) Scope of the invention. The scope of the invention is broad. The claims read on any pharmaceutical composition for treatment of any undisclosed disease which may be associated with expression of CRSP-2. The claims read on any of millions of different polypeptides which are within the homology limits recited by applicants or are capable of hybridizing to SEQ ID NO:5 under the recited hybridization conditions.

5) Amount of guidance provided. Neither applicant nor the prior art provides any disclosure on the specific biological properties of SEQ ID NO:5. In the absence of any disclosure on said biological properties, the skilled artisan would need to conduct extensive further research to determine what specific biological properties SEQ ID NO:5 possesses before even attempting to use this polypeptide as a pharmaceutical agent or attempting to identify agents which modulate the biological activity of the polypeptide. With regard to polypeptides which are homologous to SEQ ID NO:5 or comprise portions of SEQ ID NO:5 or are encoded by nucleic acids capable of hybridizing to

sequences encoding SEQ ID NO:5 and are claimed without any biological function, applicants have provided no disclosure on how one of skill in the art would use these molecules.

6) Nature of the invention. The invention involves an uncharacterized protein (CRSP-2, SEQ ID NO:5), use of said protein as a pharmaceutical agent, methods of identifying compounds that modulate activity of the protein and use of polypeptides homologous to or comprising portions of or encoded by nucleic acid sequences capable of hybridizing to sequences encoding SEQ ID NO:5 but without the functions of SEQ ID NO:5.

7) Level of skill in the art. The level of skill in the art is high; however, given the unpredictability of the art, the poorly developed state of the art with regard to the biological functions of CRSP-2, the lack of guidance on how the skilled artisan would use CRSP-2 in a pharmaceutical composition, etc., it must be considered that the skilled artisan would have had to have conducted essentially trial and error experimentation in order to identify the specific biological activities of CRSP-2 and only then begin to determine how to use the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is allowable, it must be considered that the skilled artisan would have needed to have conducted undue and excessive experimentation in order to practice the claimed invention.

The Drawings filed 1/20/98 are objected to because Figures 1-6 and 8 contain numbers, letters and reference characters that are not at least .32 cm (1/8 inch) in height (See 37 CFR 1.84(p)(3)). Objections to the Drawings will not be held in abeyance.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
July 20, 2004

DAVID GUZO
PRIMARY EXAMINER